Katare is primarily concerned with the preparation of pharmaceutical formulations of bisphosphonates by wet granulation techniques. See, for example, page 2, lines 10-13. Indeed, nearly the entire disclosure is concerned with the preparation of tablets of bisphosphonates, primarily alendronate sodium, using wet granulation techniques. At page 6, lines 15-33, the reference provides a list of bisphosphonates that can be formulated by the wet granulation process described therein. At page 10, lines 15-19, the reference provides a list of conditions that can be treated with the disclosed compositions. The list includes metastatic bone disease among other conditions.

Katdare suggests uses of oral formulations of bisphosphonates that includes the treatment of metastatic bone disease, a condition that the skilled artisan would recognize as potentially benefiting from the known bone resorption inhibition properties of bisphosphonates. The present claims are limited to the intra-arterial use of bisphosphonates for the embolic treatment of angiogenesis. Applicants assert that a disclosure suggesting the oral use of bisphosphonates for the treatment of metastatic bone disease does not anticipate their intra-arterial use in order to treat angiogenesis. Moreover, such a disclosure does not render the presently claimed invention obvious over 35 USC 103 because nothing in it even suggests that intra-arterial injection of a bisphosphonate would have any effect on angiogenesis, much less the embolic effect that the present inventors discovered.

For the reasons discussed above. Applicants request the withdrawal of all art rejections over Katdare.

Claims 1-8 are rejected under 35 USC 102(e) as anticipated by or under 35 USC 103 as obvious over Reska et al (US 6,416,964). Applicants request reconsideration and withdrawal of these rejections for the reasons that follow.

Reska et al indicates that bisphosphonates as a class activate the kinases Mst-1, Mst-2, a 34kDa kinase, a 50kDa kinase and a 130 kDa kinase. Based on this profile, the reference concludes that the bisphosphonates will have activity against angiogenesis. However, the reference fails to even suggest that the bisphosphonate should be administered intra-arterially in order to treat angiogenesis. Thus, it does not anticipate the presently claimed invention.

Moreover, nothing in the reference suggests that the bisphosphonate compound should be administered by any technique other than its usual route of administration. According to an

electronic search of the Orange Book, alendronate sodium, etidronate disodium, tiludronate disodium, risedronate sodium, pamidronate disodium and zolendronic acid are bisphosphonate products that are approved in the United States. The first four are administered orally, and the last two are administered by an intravenous infusion. As far as Applicants are aware, intra-arterial adminstration is not an approved administration route for any bisphosphonate. Therefore, Applicants further assert that the Reska et al reference, in view of what is known about the administration of bisphosphonates generally, also fails to provide any hint that the treatment of angiogenesis with bisphosphonates should be done via intra-arterial administration.

The Examiner bases the obviousness rejection over Reszka et al on the unsupported contention that finding the optimal dosage delivery system is something within the skill of the artisan. However, Applicants assert that nothing in the reference even suggests that bisphosphonates should be administered intra-arterially or that such intra-arterial administration could result in the embolic treatment of angiogenesis. The lack of such disclosure in the reference renders the present invention unobvious over the reference, especially in view of what is known about the administration of bisphosphonates generally. Accordingly, Applicants further assert that the reference does not render obvious the presently claimed invention.

For the reasons discussed above, Applicants request withdrawal of the art rejections over Reszka et al.

Entry of this amendment and reconsideration and allowance of the claims are earnestly solicited.

Respectfully submitted,

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